IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:	**DRE-0055**
Inventors:	**Laurencin et al.**
Serial No.:	**09/878,641**
Filing Date:	**June 11, 2001**
Examiner:	**Isabella, David J.**
Group Art Unit:	**3738**
Title:	**Ligament Replacement Constructs and Methods for Production and Use Thereof**

Commissioner for Patents
P.O. Box 1450
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Dear Sir:

Declaration by Dr. Cato T. Laurencin

I, Cato T. Laurencin, hereby declare:

1. I am a co-inventor of the above-referenced patent application.

2. I am very familiar with the teachings of Wolowacz (WO 95/01810) as well as other art references relating to ligament replacement constructs formed of two-dimensional (2-D) braided scaffolds as well as knitted and woven scaffolds. There are disadvantages of 2-D braided, knitted, or woven scaffolds which our invention, a three-dimensional (3-D) braided scaffold overcomes.

3. Some of the textile techniques used to fabricate ACL replacements include axial fiber structures, woven structures, knitted structures and 2-D braids. Examples of axial fiber replacements include ABC (Surgicraft, UK) a carbon based total ligament replacement and a collagen based scaffold developed by Dunn and associates (1-3).

Axial fiber replacements are structures with one or more fibers plied and fixed parallel to each other. The disadvantages of this textile structure include axial splitting due to flexural and torsional fatigue and surface peeling due to yarn on yarn and yarn on bone abrasion (4). Examples of woven fibrous ACL replacements include the Stryker and Lygeron ligament replacements (2;5;6). Woven structures are 2-dimensional interlaced yarn systems with an over and under weave pattern. The disadvantage of this textile structure is low extensibility, axial splitting, poor collagen infiltration with no orientation and abrasive wear due to tight weaving (7). Examples of knitted fibrous replacements are LARS and Stryker ligaments (2;5;6;8;9). These structures are made by interlocking a series of loops of one or more yarns to create a porous fabric to allow tissue ingrowth into the replacements. The disadvantages of knitted fabrics include surface peeling due to yarn to yarn abrasion and bone to yarn abrasion, lack of orientation of collagen tissue and the need for inner core reinforcement due to lower loading capacity. Examples of 2-dimensional braids used in ACL replacement include the Gore-Tex, Proflex and Kennedy LAD devices (2;5;6;10;11). The 2-D braided fabrics are made by using two braiding yarns in the through thickness direction of the braid. The advantage of this structure is the ability to transfer higher loads and provide for structural elongation. The disadvantages of the 2-D braided structures include tightly braided structures that inhibit collagen filtration to a few layers; collagen infiltration caused loss of structural integrity, surface peeling, axial splitting of fibers and stability issues with side-to-side displacement.

4. Our 3-D braided scaffolds exhibit superior properties for ligament replacement as compared to these other products. Previous ligament prostheses have been made of flexible composites consisting of fibers that have been woven or braided into structures. These composite structures have had problems of poor tissue integration, poor abrasion resistance and fatigue failure. The 3-D braided structures can overcome some of these problems through the development of an interconnected network of porous structures that will help the transportation of oxygen and nutrients throughout the implant site. The flexible, porous 3-D braids will allow the regeneration of new tissue between the pores and serve as scaffolds for cell proliferation. These 3-D fibrous braids besides being scaffolds for biochemical processes must also handle the

biomechanical stresses of ligaments. In addition, these 3-D braided structures are suitable for this application because they are more durable to fatigue and impact resistance compared to the 2-D braided composites due to its through thickness properties. This gives the 3-D braided structures high damage resistance during the initial implantation period as the body adjusts to the implant. Therefore, the circular and rectangular 3-D braided processes mentioned above have the properties that would be beneficial to the construction of an artificial ligament replacement. The 3-D braids have sufficient strength in the longitudinal directions, high flexibility and are resistant to damage that normally causes severe fragmentation in other braided structures that are placed in the body. The biasing of the interlacing yarns can also make 3-D scaffolds conformable, shear resistant and tolerant to impact damage (12-18).

5. Further, our 3-D braided scaffolds exhibit superior properties with respect to cell ingrowth as compared to 2-D braided scaffolds of the same material. We performed experiments with seeded ACL (anterior cruciate ligament), MCL (medial cruciate ligament), achilles tendon, and patellar tendon cells seeded at a density of 2,000 cells/cm^2, 80,000 cells /scaffold for 2-D rectangular scaffolds and 250,000 cells /scaffold for 3-D square scaffolds. The data from these studies is depicted in Figures 1 and 2, respectively. When the cell growth on each type of scaffold at 14 days was normalized by dividing total number of cells by the number of cells seeded onto the scaffolds, the cell growth is higher on the 3-D scaffolds for every cell type (Table 1).

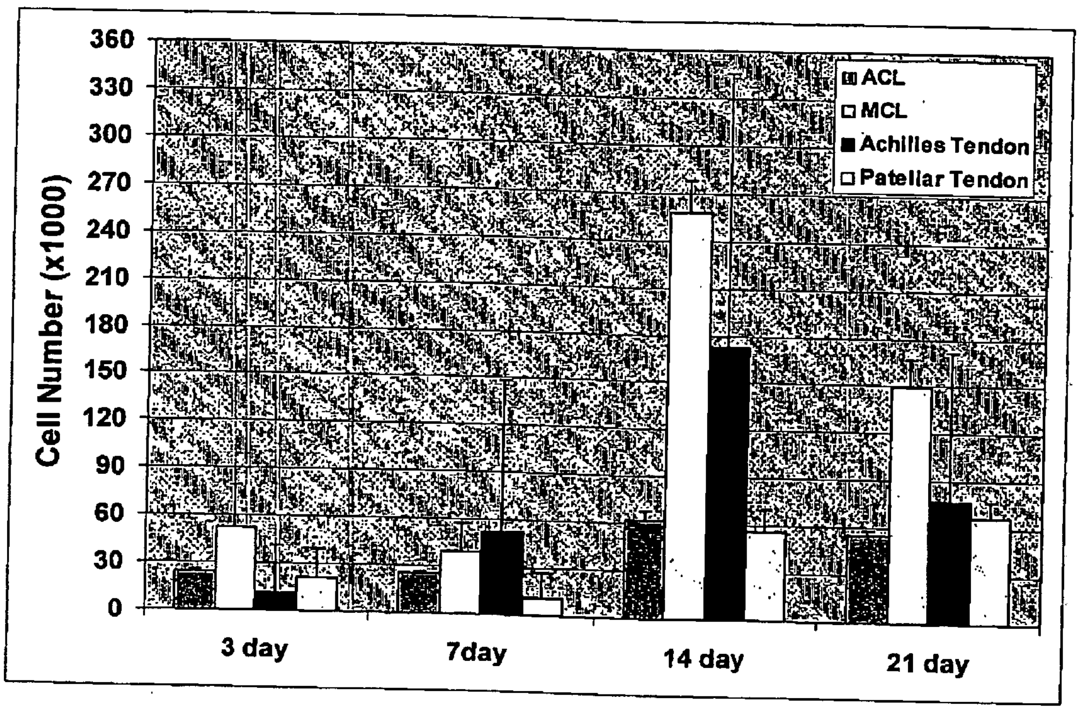

Figure 1. The cellular proliferation for 3, 7, 14 and 21 days on 2x6 2-D braid scaffolds (n = 3) (note: all cells showed significant differences within cell type group except for achilles tendon and between groups except for 7 day time point ($p < 0.05$))

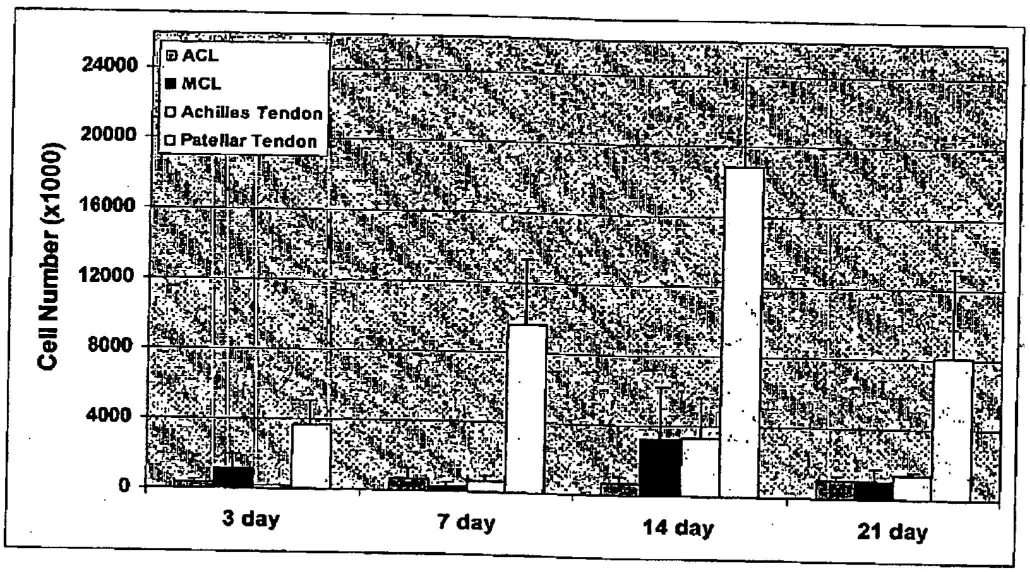

Figure 2. The cellular proliferation for 3, 7, 14 and 21 days on 5x5 PLLA 3-D square braids (n = 3) (note: significant difference within cell type group and between groups ($p < 0.05$))

Cell Type	2-D scaffolds	3-D scaffolds
MCL	3.1875	14
Achilles Tendon	2.125	14
ACL	0.75	4
Patellar Tendon	0.75	74

Table 1. Normalized amount of cell growth on each scaffold. These values were calculated by dividing total number of cells by the number of cells seeded onto the scaffolds

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I hereby declare that all statements herein of my own knowledge are true and that all statements made on information or belief are believed to be true; and further that these statements were made with the knowledge that willful statements and the like so made are punishable by fine or by imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful statements may jeopardize the validity of the application, any patent issuing there upon, or any patent to which this verified statement is directed.

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Cato T. Laurencin

_____*9/26/06*___________________________
Date